REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claims 1-10, 12 and 13 are pending in this application.

I. Claim Amendments

Claims 1 and 13 have been amended to recite "an active ingredient consisting of (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid or a pharmacologically acceptable acid addition salt thereof". Similarly, claim 10 has been amended to recite that (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid monobenzenesulfonate is "the only active ingredient". Support for these amendments can be found on page 2, line 18 to page 3, line 1, page 6, lines 4-7 and 22-25, and Experimental examples 1 and 2.

II. Personal Interview

Applicants appreciate the courtesies extended to Applicants' attorney by Examiner Frazier and Examiner Channavajjala during the personal interview held October 6, 2010.

During the interview, Applicants' attorney proposed to amend claims 1, 10 and 13 to replace "comprising" with "consisting essentially of" in order to exclude any active ingredients other than (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid (i.e., bepotastine) or a pharmacologically acceptable acid addition salt thereof, from being included in the aqueous liquid preparation of claim 1 and the aqueous eye drop of claims 10 and 13.

Applicants' attorney took the position that Stevenson et al. disclose a composition comprising **idoxuridine** and/or **cromoglycate**, and that idoxuridine and cromoglycate are known to be sensitive to light and should be protected from direct sunlight, as evidenced by the attached AHF Drug Information reference. Applicants' attorney asserted that one of ordinary skill in the art would recognize that the addition of idoxuridine or cromoglycate into a liquid preparation comprising bepotastine and sodium chloride would affect the light-stabilizing properties of the aqueous liquid preparation.

The Examiners did not find the proposed amendments and arguments to sufficiently exclude idoxuridine and cromoglycate, and they suggested amending claim 1 to recite "an active ingredient **consisting of** (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid or a pharmacologically acceptable acid addition salt thereof". The Examiners indicated that

amending the claims to recite "consisting of", rather than "consisting essentially of", would distinguish the claimed invention over Stevenson et al.

Accordingly, claims 1, 10 and 13 have been amended in accordance with the Examiners' suggestion.

Applicants' attorney also asserted that the enclosed ALBALON package insert teaches that a solution of sodium salt and antazoline should be kept in the shade, and that one of ordinary skill in the art would have found that sodium chloride has no effect on light stability of an antihistamine, such as antazoline. Applicants' attorney also argued that one of ordinary skill in the art would have recognized that an antihistamine, such as antazoline, does not have light-stabilizing properties. Therefore, Applicants' attorney asserted that one of ordinary skill in the art would have had no reason to combine the bepotastine disclosed in Kita et al. with the composition of Stevenson et al.

The Examiners asserted that the references were combined, because Stevenson et al. teach that antihistamine compounds can be added to the compositions, and Kita et al. teach that bepotastine is a particularly suitable compound for medical use because it has excellent physiochemical stability.

Applicants have carefully considered the Examiners' comments, and have amended the claims and provide the following additional remarks in consideration thereof.

III. Claim Rejection Under 35 U.S.C. § 103

The Examiner rejects claims 1-10, 12 and 13 under 35 U.S.C. 103(a) as being unpatentable over Stevenson et al. (U.S. 4,053,628) in view of Kita et al. (U.S. 6,307,052). As applied to the amended claims, Applicants respectfully traverse the rejection.

As discussed above, Stevenson et al. disclose a clear composition comprising 1,3-bis(2-carboxychromon-5-yloxy)propan-2-ol (i.e., idoxuridine) and/or 5,5'-[[5,5'-(2-hydroxytrimethylene)dioxy]bis-[4-oxo-4H-1-benzopyran-2-yl]]tetrazone (i.e., cromoglycate), and the reference discloses a formulation comprising 0.56% or 0.42% sodium chloride (see col. 1, lines 29-37, and Examples 1 and 3). Accordingly, the reference clearly teaches idoxuridine and/or cromoglycate as active ingredients in the compositions, and does not disclose or suggest a composition without idoxuridine and/or cromoglycate (see, in particular, col. 1, line 31).

However, in the present application, claim 1 recites an aqueous liquid preparation comprising "**an active ingredient consisting of**" bepotastine or a pharmacologically acceptable

acid addition salt thereof"; claim 10 recites "(+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid monobenzenesulfonate, **as the only active ingredient**"; and claim 13 recites an aqueous eye drop comprising an active ingredient "**consisting of**" bepotastine or a pharmacologically acceptable acid addition salt thereof".

Accordingly, claims 1, 10 and 13 clearly exclude idoxuridine and/or cromoglycate as active ingredients, which are disclosed as active ingredients in the compositions disclosed in Stevenson et al. **The presently claimed invention is directed to a light-stabilized aqueous liquid preparation comprising an active ingredient consisting of bepotastine, and a metal chloride. The present invention contains bepotastine, or a pharmaceutically acceptable salt, as the only active ingredient, and thus does not contain any other active ingredients.**

Accordingly, one of ordinary skill in the art would not have had any reason to combine Stevenson et al. with Kita et al. to arrive at the presently claimed invention.

Furthermore, Stevenson et al. disclose that the composition may contain an antihistamine, such as **antazoline** and **diphenhydramine** (see col. 3, lines 10-16). However, claims 1, 10 and 13 exclude antazoline and diphenhydramine, because they are active ingredients (i.e., antihistamines).

As discussed above, the presently claimed invention is directed to a **light-stabilized aqueous liquid preparation** comprising an active ingredient consisting of bepotastine, and a metal chloride. Applicants take the position that both idoxuridine and cromoglycate are known to be **unstable to light** (See AHF Drug Information, IDU Ophth. Soln. 0.1% KAKEN™). Stevenson et al. do not disclose a technique to light-stabilize these compounds with a metal chloride, but teach that idoxuridine Ophth. Soln. (IDU Ophth. Soln.) requires preservation in shading, even if it contains sodium chloride. Applicants enclose a copy of a web page explaining Herplex-D, an idoxuridine preparation (see http://www.paylessonlinepharmacy.com/customer/product-1342-Herplex-D-Idoxuridine-Topical-Solution.html).

From this disclosure, one of ordinary skill in the art would recognize that if idoxuridine or cromoglycate were added to an aqueous composition, then the composition would have **inferior light stability**, irrespective of the presence or absence of a metal chloride. Therefore, one of ordinary skill in the art would not have had any reason to use bepotastine, as disclosed in Kita et al., in place of the antihistamine disclosed in Stevenson et al., to make an aqueous liquid preparation capable of solving the light stability problems addressed in the present application.

Therefore, claims 1, 10 and 13 would not have been obvious over the references.

Claims 2-9 and 12 depend directly or indirectly from claim 1, and thus also would not have been obvious over the references.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

IV. Conclusion

For these reasons, Applicants take the position that the presently claimed invention is clearly patentable over the applied references.

Therefore, in view of the foregoing amendments and remarks, it is submitted that the rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

Masayo HIGASHIYAMA

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Enclosures:
1) AHF Drug Information
2) ALBALON package insert
3) Print out from: http://www.paylessonlinepharmacy.com/customer/product-1342-Herplex-D-Idoxuridine-Topical-Solution.html